mismatched related (MRD) donors have increased the incidence of CMV infection and disease. **Methods:** Twenty-four (24) out of 50 patients have been enrolled into a prospective trial evaluating the safety and efficacy of valganciclovir for the early prophylaxis of CMV infection. Patients are either CMV seropositive or CMV seronegative receiving CMV seropositive stem cell products. Other inclusion/exclusion criteria include estimated creatinine clearance of ≥ 50 mL/min, platelet count ≥ 50,000/μL, and WBC count ≥ 1,000/μL. Patients receive valganciclovir at 900 mg daily Mondays through Fridays starting 21–35 days after transplantation and continuing through posttransplantation day 100, with dosage adjustments for myelosuppression and/or reduced creatinine clearance. Patients are monitored with weekly CMV PCR analysis performed at a central laboratory. **Results:** All patients were CMV seropositive at the time of transplant. Donors included 15 MRD and 9 MUD. Stem cell sources included 21 peripheral blood and 3 bone marrow. Seven patients required corticosteroids for treatment of graft-versus-host disease. Three patients developed myeloid toxicity related to valganciclovir (absolute neutrophil count < 1,000/μL in 1 patient and platelets < 50,000/μL in 2 patients). All 3 patients recovered their counts and restarted valganciclovir with dosage adjustments. A total of 11 patients required dosage adjustments due to myelosuppression (in 3 patients), creatinine clearance (in 4), weight (in 1), or institutional decision (in 3). CMV infection occurred in 2 patients; no patients developed CMV disease. The 2 patients with positive CMV-PCR developed infection 1 (day 40) and 2 (day 36) weeks after starting valganciclovir. These 2 patients were successfully treated with IV ganciclovir. So far, 10 patients have been followed between day +100 and 6 months posttransplantation; of these, 3 continued valganciclovir off study. Of these 10 patients, 2 developed CMV infection. Both patients were not receiving CMV prophylaxis and were successfully treated with valganciclovir. None of the 3 patients that continued valganciclovir up to 6 months posttransplantation developed CMV infection. Survival is 80% (16 of 20) at day +100 and 82% (9 of 11) at 6 months posttransplantation. **Conclusions:** We conclude that valganciclovir at the dosage used in this study is well tolerated with minimal reversible myelosuppression. The early prophylaxis and suppression of CMV viremia correlates favorably with preemptive strategies.

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PREEMPTIVE THERAPY WITH GANCICLOVIR AND SHORT-COURSE INTRAVENOUS IMMUNOGLOBULIN DOES NOT PREVENT RECURRENT CYTOMEGALOVIRUS INFECTION (CBMTG-102 STUDY)

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Background: Cytomegalovirus (CMV) infection continues to be a significant problem following allogeneic hematopoietic stem cell transplantation. Preemptive therapy with ganciclovir (GCV) reduces the incidence of CMV disease, but 20%-50% of patients develop recurrent CMV infection and require further treatment. Because intravenous immunoglobulin (IVIG) increases CMV antibody titers and has proven beneficial for the treatment of CMV pneumonitis, we hypothetized that a preemptive regimen with a short course of IVIG and GCV would reduce the incidence of recurrent CMV infection. **Methods:** A 2-stage randomized phase II multicenter study was conducted with a control arm included to verify a 50% incidence of recurrent CMV infection. A total of 23 allogeneic myeloablative stem cell transplantation patients with CMV viremia, detected using CMV antigenemia asssay (in 22 patients) or CMV PCR assay (in 1 patient), were enrolled. Fifteen patients received IV GCV 5 mg/kg every 12 hours until CMV viremia had resolved (minimum 14 days) and IVIG 500 mg/kg on Monday, Wednesday, and Friday for 3 doses. Eight control patients were randomly selected to receive only GCV. Patients were followed 6 months for recurrence of CMV infection. An economic analysis was also performed. **Results:** The study was stopped after the interim analysis, because no significant decrease in recurrent CMV infection was observed. The mean age of the 15 study patients was 37.5 years. Diagnoses were 6 ALL, 3 AML, 2 myeloma, 1 MDS, 1 CML, 1 ALL, and 1 NHL. The stem cells were from peripheral blood (in 12 patients) or bone marrow (in 3 patients), with 80% from HLA-matched donors. Positive CMV serology was present in 10 donors and 13 recipients pretransplantation. CMV viremia was detected a median of 41 days (range, 26–243 days) posttransplantation. Recurrent CMV viremia has occurred in 8 of 15 patients (53%). This was similar to the control arm, in which 3 of 8 patients (43%) developed CMV recurrence and 1 patient (14%) failed GCV therapy. Acute GVHD occurred in 73% of patients and chronic GVHD in 83% of patients during the 6-month study period. Thirteen patients were alive at last follow-up, and 2 patients had relapsed hematologic disease. The economic analysis indicates that patients receiving GCV and IVIG developed more infectious complications requiring hospital admissions, which resulted in a significantly higher overall cost compared to control patients. **Conclusions:** The addition of a short course of IVIG to GCV for preemptive therapy of CMV infection does not reduce the incidence of recurrent CMV infection.

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PHASE I TRIAL OF CG53135-05 TO PREVENT MUCOSITIS IN PATIENTS UNDERGOING HIGH-DOSE CHEMOTHERAPY (HDCT) AND AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION (PBSCT)

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Mucositis is a painful side effect of many transplantation conditioning regimens and often requires treatment with potent narcotic pain medications. It may even require intravenous patient-controlled analgesia (PCA) for adequate pain relief, as well as total parenteral nutrition (TPN). Recently, a new class of drugs in the fibroblast growth factor (FGF) family has shown promise in more effectively ameliorating or even preventing oral mucositis (OM). We report on the results of a phase I trial with CG53135-05, a novel investigational protein therapeutic (FGF-20) that promotes epithelial and mesenchymal cell proliferation in vitro and has demonstrated activity in animal models. A total of 22 patients (age range, 25–75 years) undergoing HDCT with PBSCT were treated with escalating doses of study drug, including 0.03 mg/kg in 2 patients, 0.1 mg/kg in 10, 0.2 mg/kg in 8, and 0.33 mg/kg in 2. Patients were treated for multiple myeloma in 11, non-Hodgkin's lymphoma in 9, acute myelogenous leukemia in 1, and desmoplastic round cell tumor in 1 and received conditioning regimens including melphalan (Mel 200); cyclophosphamide, carmustine, and etoposide (CBV); carboplatin and thiotepa (CT); and busulfan/cyclophosphamide (targeted BuCy). The primary objective of the trial was to evaluate safety, tolerability, and pharmacokinetics of CG53135-05. Patients were also scored daily for presence of OM.

Among the 22 patients completing the study, 8 patients experienced no OM (including 4 Mel 200 patients), 10 patients experienced only WHO grade 1 (n = 7) or grade 2 (n = 3) OM, and 4 patients experienced severe OM of grade 3 (n = 3) or grade 4 (n = 1). One patient experiencing grade 4 OM required TPN for 4 days. Patients tolerated the study drug well with no significant side effects up to a dose of 0.33 mg/kg. At that dose, 2 patients experienced an infusional reaction consisting of fever, nausea, and mild hypotension. Preliminary pharmacokinetic results from 13 patients confirmed dose-dependent plasma exposure with an average C_{max} of 135.5 ng/mL at a dose level of 0.1 mg/kg, 343.3 ng/mL at 0.2 mg/kg, and 658.3 ng/mL at 0.33 mg/kg.

CG53135-05 is a member of a breakthtrough drug class (FGF family) that was well tolerated in PBSCT patients at doses up to 0.33 mg/kg with apparent clinical effects in ameliorating or preventing OM. Thus 18 of 22 patients avoided (WHO grades 3–4) mucositis following HDCT. A larger phase II clinical trial will be initiated to evaluate the efficacy of CG53135-05 in preventing HDCT-induced OM.